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GUEST EDITORIAL

Photodynamic Therapy in Barrett's High-Grade Dysplasia: Are We Ready To Abandon Esophagectomy for a More Conservative Therapy?

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The diagnosis of high-grade dysplasia (HGD) occurring in Barrett's metaplasia of the esophagus has been accepted, in surgical circles, as a clear indication for esophagectomy [1]. The rationale for the operation, with its well-established high morbidity and mortality, has been the large number of unsuspected invasive carcinomas as well as the much better survival of these patients as compared with the average patient with esophageal carcinoma [2,3]. The difficulty with this approach is that a large number of patients, without a life-threatening cancer, are subjected to a major, morbid, and disabling operation and a few may die from the procedure [1,4]. In addition, many elderly patients are not candidates for surgery due to poor medical condition and receive no treatment at all.

Some investigators have advocated a more conservative approach of close follow-up evaluation with four quadrant biopsies every 2 cm throughout the entire length of the Barrett's metaplasia in conjunction with aggressive medical therapy for the gastroesophageal reflux. With this approach, only patients who progress to an invasive adenocarcinoma require surgery. With this approach, up to 76% of the patients are spared from surgery [5,6].

A new therapeutic modality, photodynamic therapy (PDT) is now being tried at various centers in the United States in Barrett's with HGD and early carcinomas. This treatment introduced in the clinical arena by Dr. Thomas J. Dougherty at Roswell Park Cancer Institute 25 years ago [7], was approved by the Food and Drug Administration (FDA) in 1995 for the palliative treatment of obstructing esophageal tumors and in January 1988 for the treatment of early bronchial cancer. PDT consists of a cytotoxic reaction produced by a photosensitizer, (Photofrin®, porfimer sodium QLT Phototherapeutics, Vancouver, BC, Canada), which, when injected, is selectively retained by the neoplastic tissue much longer than by the normal surrounding tissues. The toxic reaction is triggered by exposing the tissues to an intense red light at 630 nm of wave length causing the release of a reactive form of oxygen (singlet oxygen) [8]. Initial experience with PDT in the Far East suggested complete response and prolonged control of early invasive tumors of the esophagus, stomach, and bronchus [9,10].

Our group experience with PDT in HGD began in 1987 when a 40-year-old white man rejected surgery and accepted PDT as experimental therapy. His response to the endoscopically delivered PDT was complete sloughing of the entire Barrett's mucosa, followed, over the next seeral months, with the gradual replacement by squamous mucosa. Although small tongues of Barrett's remained at the lower esophagus, his HGD was erradicated. Two more patients with Barrett's HGD were treated with PDT with similar response. This pilot experience was presented at the 1990 Third Biennial Meeting of the International Photodynamic Therapy Association in Buffalo, New York [11].

In 1993, Overholt et al. [12] reported good early response in two patients with early carcinoma arising in Barrett's noting reduction of the length of the Barrett's after PDT. By 1997 the same group reported their cumulative experience with 55 patients. Thirty-six of those patients had HGD, and in 24 patients this was eliminated with 7 of them showing no residual Barrett's. An addi-

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tional nine patients converted to a low-grade dysplasia and in three the HGD persisted [13].

Wang et al. [14] have reported six HGD patients, with 5 showing complete elimination of the dysplasia. At Roswell Park Cancer Institute, our accumulated experience of 10 patients with HGD was recently reviewed. All patients had initial necrosis of the Barrett's mucosa, in seven cases complete elimination of HGD was achieved, and three patients had persistent or developed recurrent HGD after 4, 8, or 66 months [15].

A major concern when treating patients nonsurgically is the risk of overlooking early invasive carcinoma, which can allow the tumor to progress and metastasize. This risk has to be weighed against the morbidity and mortality associated with surgical resection [16,17].

The relatively good success with PDT in Barrett's with HGD has generated interest to test this treatment in a multicenter prospective randomized study that is being organized and sponsored by QLT Phototherapeutics. We expect that this study will help us redefine and establish the role of PDT as part of the multidisciplinary approach in the management of this condition.

It is apparent that PDT has the capacity of producing mucosal ablation of the Barrett's mucosa harboring dysplasia and early adenocarcinomas. The completeness and duration of response need to be prospectively evaluated before PDT becomes an accepted modality in the management of this disease.

REFERENCES

1. Skinner DB, Belsey RH (eds): ''Management of Esophageal Disease.'' Philadelphia: WB Saunders, 1988.
2. Heitmiller RF, Redmond M, Hamilton SR: Barrett's esophagus with high-grade dysplasia. An indication for prophylactic esophagectomy. Ann Surg 1996;224:66–71.
3. Edwards MJ, Gable DR, Lentsch AB, et al.: The rationale for esophagectomy as the optimal therapy for Barrett's esophagus with high-grade dysplasia. Ann Surg 1996;223–225;585–591.
4. Reid BJ, Weinstein WM, Lewin KJ, et al.: Endoscopic biopsy can detect high-grade dysplasia or early adenocarcinoma in Barrett's esophagus without grossly recognizable neoplastic lesions. Gastroenterology 1998;94:81–90.
5. Levine DS, Haggitt RC, Blount PL, et al.: An endoscopic biopsy protocol can differentiate high-grade dysplasia from early adenocarcinoma in Barrett's esophagus. Gastroenterology 1993;105:40–50.
6. Schnell T, Sontag SJ, Chejfec G, et al.: High-grade dysplasia (HGD) is not an indication for surgery in patients (pts.) with Barrett's esophagus (BE). Gastroenterology 1996;110:A-590.
7. Dougherty TJ, Kaufman JE, Goldfarb A, et al.: Photoradiation therapy for the treatment of malignant tumors. Cancer Res 1978;38:2628.
8. Henderson BW, Dougherty TJ: How does photodynamic therapy work? Photochem Photobiol 1992;55:145–157.
9. Hayata T, Kato H, Okitsu H, Kawaguchi M, Konoka C: Photodynamic therapy with hematoporphyrin derivative in cancer of the upper gastrointestinal tract. Semin Surg Oncol 1985;1:1–11.
10. Tian ME, Qui SL, Ji Q: Preliminary results of hematoporphyrin derivative laser treatment for 13 cases of early esophageal carcinoma. Adv Exp Med Biol 1985;193:21–25.
11. Nava H, Zera R, Douglass HO, et al.: Photodynamic therapy in carcinoma in situ in Barrett's esophagus. Third Biennial International Photodynamic Association Meeting, Buffalo, New York, July 1990 (abst).
12. Overholt B, Panjehpour M, Tefftellar E, et al.: Photodynamic therapy for treatment of early adenocarcinoma in Barrett's esophagus. Gastrointest Endosc 1993;39:73–76.
13. Overholt BF, Panjehpour M: Photodynamic therapy for Barrett's esophagus. Gastrointest Endosc Clini North Am 1997;7:207–220.
14. Wang KK, Wong Kee Song LM, Nourbakhsk A, et al.: Can consistent tissue necrosis be achieved during photodynamic therapy for high-grade dysplasia or cancer within Barrett's esophagus. Gastroenterology 1997;112:A676.
15. Nava HR, Douglass HO, Smith J, et al.: Efficacy and complications of photodynamic therapy (PDT) in Barrett's esophagus with severe dysplasia (SD) or carcinoma in situ (CIS). Sixth International Congress of European Association for Endoscopic Surgery (EAES), June 1998, Rome, Italy (abst).
16. Rice TW, Falk GW, Achkar E, et al.: Surgical management of high-grade dysplasia in Barrett's esophagus. Am J Gastroenterol 1993;88:1832–1836.
17. Sibille A, Lambert R, Souquet J, et al.: Long-term survival after photodynamic therapy for esophageal cancer. Gastroenterology 1995;108:337–344.